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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,505	07/31/2001	Walter Ausserer	100/11630	2767

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EXAMINER	
BARTON, JEFFREY THOMAS	
ART UNIT	**PAPER NUMBER**
1753	

DATE MAILED: 03/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/919,505	AUSSERER ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Barton	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed on 21 December 2005 does not place the application in condition for allowance.

Status of Objections and Rejections Pending Since the Office Action of 29 September 2005

2. All objections and rejections of claims 28-31 and 48-54 are obviated due to cancellation of the claims.

3. The objection to claim 8 is withdrawn due to Applicant's amendment.

4. The rejection of claims 1-8, 10-13, 15, and 16 under 35 U.S.C. §102(b) as anticipated by Dubrow et al is withdrawn due to Applicant's amendment.

5. The rejection of claim 9 under 35 U.S.C. §103(a) as unpatentable over Dubrow et al in view of Taylor is withdrawn due to Applicant's amendment.

6. The rejection of claim 17 under 35 U.S.C. §103(a) as unpatentable over Dubrow et al in view of Ramsey is withdrawn due to Applicant's amendment.

7. All other previous grounds of rejection are maintained.

Claim Objections

8. Claim 1 is objected to because there is no antecedent basis for "the separation conduit" in lines 15-16 and line 19 of the claim. It appears that "the separation channel"

was intended, and the claim is treated as such herein. Appropriate correction is required.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-8, 10-18, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dubrow et al (WO 98/49548) in view of Soper et al.

Regarding claim 1, Dubrow et al disclose a method of separating sample materials into fractions, comprising: (a) providing a system comprising: a separation channel having a separation matrix disposed therein (Figure 1, channel 100; Page 7, lines 22-25); an injection channel (Figure 1, portion of channel 102 between load/waste channels 114 and 116) in fluid communication with the separation channel at an intermediate point along the injection channel; a sample loading channel in fluid communication with the injection channel (e.g. Channel 106 as shown in panels II and III of Figure 1C); a source of a first sample material (e.g. reservoir 112); and a source of reagent (Page 15, lines 5-7; such reagents must be introduced through other reservoirs/channels communicating with channel 102); (b) transporting the first sample material and reagent into the sample loading channel wherein the first sample and reagent form a mixture (Preloading step with added reagent: Figure 1C, panel II; Page 14, lines 7-15; Page 15, lines 3-7); (c) injecting a portion of the mixture from the sample loading channel through the injection channel into the separation channel (Figure 1C, panels III and IV); (d) separating the first sample material within the mixture into a plurality of fractions (Page 7, lines 22-25; since "fractions" are simply portions of a whole, the separation reads on this step); and (e) transporting a second sample material

into the sample loading channel. (Figure 1C, panels II and III and Figure 2; Page 14, lines 7-8; numerous samples are run, each with the preload/load steps)

Regarding claims 2 and 8, Dubrow et al disclose the sample loading channel (Channel 106 as shown in panel II of Figure 1C) comprising a loading end (At reservoir 112) and a waste end (downstream end, towards the waste reservoir), the loading end being contacted with a source of the first sample material (Sample source 112) through a capillary element (Channel 106, itself), and further comprising applying a first pressure difference across the sample loading channel as claimed. (Column 16, lines 22-27; material transport by applied pressure is disclosed)

Regarding claims 3-5, with pressure driven flow from reservoir 112 to reservoir 120, the displacement of the separation matrix in channel 100 would depend on the relative flow resistances of the channels (e.g. 106, 116, 100), fluid viscosities, etc. For a separation channel with significantly higher flow resistance than the sample loading channel (i.e. much longer, as in the device shown in Figure 3), displacement of the amounts claimed would inherently result. In addition, the step shown in Panel III of Figure 1C is also a step that involves injecting sample material from the reservoir 112 into the sample loading channel 106, and such a flow path would clearly displace matrix material located in the separation channel at its intersection with the injection channel.

Regarding claims 6 and 7, the separation channel (100) of Dubrow et al (see also Figure 3, separation channel 304) has a greater length, and therefore greater flow resistance than the sample loading channel, since all channels are disclosed as having similar cross-sectional dimensions. (Page 19, lines 19-23)

Regarding claim 10, Dubrow et al disclose the injection channel (Portion of channel 102 between load/waste channels 114 and 116) and separation channel (100) being in fluid communication at a first fluid junction (108), and a method further comprising moving a portion of the first sample material in the injection channel through the first fluid junction and into the separation conduit. (e.g. Figure 1C, panels III and IV)

Regarding claims 11 and 12, Dubrow et al disclose causing fluid motion within their device using electrokinetic flow (Page 13, lines 14-19) or pressure. (Page 16, lines 22-27)

Regarding claim 13, Dubrow et al disclose performing electrophoresis to separate components of the injected sample. (Page 13, lines 19-22)

Regarding claim 14, Dubrow et al disclose the separation channel being in communication with a source of separation medium, and filling the separation channel with separation medium by applying a pressure difference. (Page 19, lines 27-34)

Regarding claim 15, Dubrow et al disclose the sample loading channel (Channels 106/102/116) being in fluid communication with the reagent source via a reagent channel (Figure 1, Page 15, lines 3-11; Within this channel geometry, the reagent disclosed must be introduced from other channels/reservoirs in communication with channel 102, e.g. to the right of the portion illustrated in figures 1A and 1C, panel II. Suitable reservoir geometries for such an arrangement are shown in Figures 3-5); and wherein the reagent channel and sample loading channel have differing flow resistances. (e.g. in the geometry of Figure 3, an analogous sample loading channel to that described above would be channels 356/358, with reagent introduced from channel

348 or 350. The lengths of these channels are different, and since they would have the same cross-sectional dimension, their flow resistances would be different.

Regarding claim 16, Dubrow et al disclose the reagent being a diluent. (Page 15, lines 5-7)

Regarding claim 18, Dubrow et al disclose analysis of subsequently injected samples. (Figures 1C and 2)

Regarding claims 26 and 27, the system of Dubrow et al is a microfluidic device with channels having microscale dimensions. (Page 19, lines 19-26)

Dubrow et al do not explicitly disclose displacement of the separation matrix from the separation channel after separating the first sample material, or displacement of the separation matrix being caused by the same force that causes movement of the second sample material into the sample loading channel. Specific to claim 17, Dubrow et al do not explicitly disclose the sample loading channel having substantially no separation matrix disposed therein.

Soper et al disclose a method comprising the step of replacing the medium in the separation channel after each electrophoresis experiment, specifically by filling the channel with new medium after each analysis. (Column 13, lines 8-39) Soper et al also disclose a microfluidic system in which separation medium is provided to the separation channel, with no disclosure of medium located within the injection channels. (Column 13, lines 8-39)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Dubrow et al by replacing the matrix after

each electrophoresis experiment, as taught by Soper et al, because it would reduce the effects of matrix contamination from previous runs, and increase the reproducibility of experiments, as would be obvious to a skilled artisan.

In such a combination, the force used to transport the second sample into the sample loading channel (i.e. Panels II and III of Figure 1c) will displace separation matrix from the portion of the separation channel lying at its intersection with the injection channel, reading on the claim.

Specific to claim 17, it would have been obvious to one having ordinary skill in the art to limit the separation medium to the separation channel, as taught by Soper et al, because there is no need for sieving of sample components prior to injection. In fact, separation media in the sample loading or injection channels could bias the injection by preventing the flow and injection of sample components which migrate slowly through the matrix. (e.g. high-MW polynucleotides) A skilled artisan would seek to avoid such injection biasing, and be motivated not to dispose sieving media in the injection or sample loading channels.

13. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dubrow et al (WO 98/49548) and Soper et al as applied to claim 2 above, and further in view of Taylor.

Dubrow et al and Soper et al disclose a method as described above in addressing claim 2.

Dubrow et al do not explicitly disclose using a vacuum or negative pressure to cause fluid flow, simply disclosing pressure-driven fluid transport at Page 16, lines 22-27.

Taylor et al disclose bulk flow of process fluids caused by application of pressure differences, including application of vacuum, to device ports and across channels in their device. (Column 2, lines 23-45; Column 6, lines 60-65)

It would have been obvious to one having ordinary skill in the art to modify the method of Dubrow et al by specifically using the application of a pressure gradient by application of vacuum to the waste port, as taught by Taylor et al, because it is a known, conventional means of causing pressure driven fluid flow in capillary devices, and would avoid sample biasing. Application of negative or positive pressure to a port to cause flow are known in the art to be equivalent means of accomplishing pressure driven flow, and the use of either would have been obvious to one having ordinary skill in the art.

14. Claims 1-8, 10-18, 26, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dubrow et al in view of Adourian et al.

The disclosure of Dubrow et al is as described above in paragraph 12.

Dubrow et al do not explicitly disclose replacing any portion of the separation matrix between runs.

Adourian et al teach the benefits of replacing the separation matrix in an electrophoresis chip, by improving reproducibility (i.e. restoring the original migration times). (Column 24, lines 2-20)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Dubrow et al by replacing the matrix after each electrophoresis experiment, as taught by Adourian et al, because it would reduce the effects of matrix contamination from previous runs, and increase the reproducibility of experiments.

15. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dubrow et al and Adourian as applied to claim 1 above, and further in view of Taylor.

The reasoning for this rejection parallels that given above in paragraph 13.

16. Claims 19-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dubrow et al and Adourian et al as applied to claim 18 above, and further in view of Nakajima et al.

Dubrow et al and Adourian et al disclose a method as described above in addressing claim 18.

Neither Dubrow et al nor Adourian et al explicitly disclose replacing only portions of the separation matrix.

Nakajima et al disclose a method of improving the performance of previously used chromatographic columns of any size (Column 2, lines 61-62) by replacing a portion of the separation matrix with fresh material. (Column 4, line 66 - Column 5, line 9) Examples are given from 4-65% replacement. (Table 1)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Dubrow et al and Adourian et al by replacing only a portion of the separation matrix after a number of runs, as taught by Nakajima et al, because it would conserve separation medium. Additionally, if performed in an automated system after each run, it would help maintain consistent run-to-run matrix performance.

Regarding claim 25, it would also be obvious to replace any fraction of the gel that would provide beneficial results, which could be determined by one of ordinary skill in the art.

Response to Arguments

17. Applicant's arguments filed 21 December 2005 have been fully considered but they are not persuasive. Applicant argues that the newly added limitations to claim 1 are neither taught not suggested by the cited prior art. The Examiner respectfully disagrees. The replacement of separation matrix taught by Soper et al and Adourian et al require the recited displacement step, and in the combination described above, the pressure-driven transport of the second sample would cause displacement of the matrix from the separation channel, after such a matrix replacement step. This reads on the claim as currently presented.

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
24 February 2006

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